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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/882,934	06/15/2001	Douglas Shytle	LAY-011CIA	9442
26158	7590	01/03/2005	EXAMINER	
WOMBLE CARLYLE SANDRIDGE & RICE, PLLC P.O. BOX 7037 ATLANTA, GA 30357-0037			JAGOE, DONNA A	
			ART UNIT	PAPER NUMBER

1614

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/882,934

Applicant(s)

SHYTLÉ ET AL.

Examiner

Donna Jágoe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 09 August 2004 and 24 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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The amendment filed 24 September 2004 has been received and entered. Claim 16 has been amended and claims 1-11 have been canceled. Claims 12-20 are pending to which the following grounds of rejection remain applicable.

The rejection made in the paper mailed 10 May 2004 under 35 U.S.C. §103(a) over Crooks in view of the Merck Manual is maintained and hereby repeated for the reasons set forth in the previous office action and those set forth below. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant asserts that "no teaching by Crooks of particular nicotinic receptor antagonists in combination with the asserted teaching of the Merck Manual could possibly render Applicants' claims unpatentable. Applicants point to the phrase "substantially free of exo-S mecamylamine in the instant specification as being defined as "the composition contains at least 90% by weight of exo-R-mecamylamine and less than about 10% by weight of exo-S-mecamylamine. As noted in the particulars of *In re ADAMSON AND DUFFIN*, 125 USPQ 233 (CCPA 1960); optical activity is attributable to asymmetric molecular structure and that synthetically produced substances containing asymmetric carbon atoms are optically inactive due to the formation of equal amounts of the dextro and levo isomers. Such compounds are said to be racemic. Karrer (*Organic Chemistry Text*) teaches that racemates may be resolved (separated) by various methods. The treatise indicates that, except for their effect on polarized light, their physiological behavior and their relative reactivity with other optical isomers, "in the case of innumerable d and l forms, the chemical and

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physical properties of those isomers have always proved to be identical.” This is so, even though the chemical and physical properties of a racemate may be substantially different than those of its stereoisomers. It further states “the physiological properties of two antipodes [stereoisomers] can differ considerably,” giving as examples, several pairs of optical isomers, which differ substantially in their physiological effects. “The cause of the different physiological behavior” it is said, “lies in the fact that many constituents of cells within the organism with which the substances react are themselves asymmetric.” The board held that the Karrer reference would lead one skilled in the art to believe that the Adamson compounds existed in the racemic form and thus were potentially separable into their optically isomeric forms, as in the instantly claimed mecamlamine. For these reasons, it was held by the board that both the compounds and the method claims would have been obvious to one of ordinary skill in the stereoisomer and pharmaceutical arts and would recognize that the Adamson compounds exist as racemates, hence the fact that no reference to stereo-isomerism is made by the Adamson references themselves is of no moment. Neither is it open to dispute that it is well known to those skilled in the art that racemic mixtures are potentially separable, for Karrer teaches that racemates may be resolved into their levo and dextro isomers by one of several methods, including the specific method utilized, though not claimed by appellants. Karrer teaches that the pharmacological activity of two stereoisomers may differ substantially because of the nature of the substances with which they react, to produce their physiological effects. The appellants argued that the compounds from which Karrer deduces that general principle are so different from their

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own levo isomers that the general rule is inapplicable here. Concededly, those compounds are different, however, the board found no reason of record to believe that Karrer's statement would not teach one of ordinary skill in the art that the optical isomers of the Adamson et al. racemates, and the quaternary ammonium salts and acid addition salts thereof, may have different spasmolytic activities. In establishing that fact experimentally appellants have done no more than what would be expected by one skilled in the art. i.e., the activities are different. The board found that the contentions based upon the properties of the claimed compounds are devoid of persuasive force upon the issue of those compounds' obviousness. The process claim 10 recited only the broad step of separating the isomers and "recovering the levo-isomer from the [racemic] mixture substantially free of the dextro-isomer," claim 11 adding to that the step of quaternizing the levo-isomer.

As stated in the office action dated 10 May 2004, Crooks et al. teach nicotine analogs that have nicotinic receptor antagonist properties, useful in treatment of cognitive disorders such as Parkinson's disease. It does not teach treatment of Tourette's Syndrome, however it would have been obvious to employ a nicotine receptor antagonist such as mecamylamine to treat symptoms of Tourette's Syndrome motivated by the teaching of Crooks et al. who teaches treatment of neurologic disorders with nicotine receptor antagonists and the teaching of the Merck manual that teaches that dyskinesias such as Tourette's Syndrome are due to basal ganglia disorders (a neurologic disorder). It is therefore reasonable to conclude that the strength of correlation between references gives rise to reasonable expectation of

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success from combining them. Regarding the exo-R-mecamylamine, substantially free of exo-S-mecamylamine, the board, in *In re Adamson*, found that the contentions based upon the properties of the claimed compounds are devoid of persuasive force upon the issue of those compounds' obviousness.

Applicant's argument regarding the date of WO 99/07378 reference is noted.

The priority of the instant application is December 16 1999. The International publication date of the WO PCT reference is February 18 1999, this appears to be nearly 10 months prior to the instant application. Therefore the rejection is maintained and hereby repeated. Applicant asserts that the USF reference fails to teach or suggest any pharmaceutical composition or treatment method using any single isomer of mecamylamine substantially free of the other isomer. In general, stereoisomers/optical isomers are obvious from racemic mixtures. As legal authority the examiner cites *In re Adamson and Duffin*, 125 U.S.P.Q. 233. The case sets forth the requirements of patentability with regard to stereoisomers as follows:

1) The existence of a racemate is, in and of itself, sufficient to render obvious any individual stereoisomers contained within; no express suggestion of isomer separation is needed. See the first paragraph on page 235.

2) One skilled in the art expects that individual stereoisomers will differ significantly in physiological/pharmacological activity and toxicity, because living systems are chiral and thus preferentially process stereochemical configurations over others. See page 234, the third full paragraph and page 235, the fifth full paragraph on the page.

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Mecamylamine is known from the recitation of WO 99/07378 and it is taught to be useful for neuropsychiatric disorders, including Tourette's syndrome. Consonant with the reasoning of *Adamson*, the existence of that racemate renders obvious any individual stereoisomers contained within, i.e. the R and S enantiomers recited instantly. It would have been obvious to one of ordinary skill in the stereoisomer and pharmaceutical arts and one would recognize that the USF compounds exist as racemates; hence the fact that no reference to stereo-isomerism is made by the USF reference itself is of no moment. Neither is it open to dispute that it is well known to those skilled in the art that racemic mixtures are potentially separable, for Karrer teaches that racemates may be resolved into their laevo-and dextro-isomers by one of several methods including the specific method utilized, though not claimed by appellants. Karrer teaches that the pharmacological activity of two stereoisomers may differ substantially because of the nature of the substances with which they react to produce their physiological effects.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

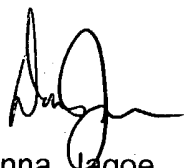
Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Donna Jagoe
Patent Examiner
Art Unit 1614

12/27/2004



CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600